REMARKS

Amendments To The Claims

Applicants have canceled claims 2, 8, 19, 22-32, 39 and 42-46 without prejudice to their right to pursue that subject matter in this or other applications, claiming the same priority as this application. These claims are directed to nonelected inventions. The Examiner has withdrawn them from consideration in this application.

Claims 20-21, 33-38, 40-41 and 47 are now pending in this application.

Applicants have amended claims 20, 21, 33, 35, 40 and 47.

None of the amendments adds new matter. They also place the claims in form for allowance or in better form for appeal. Their entry is requested.

THE OFFICE ACTION

Rejections under 35 U.S.C. § 112, Second Paragraph

Indefiniteness

Claims 20-21, 33-38, 40-41 and 47 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite.

Applicants have amended the claims, as the Examiner has suggested to overcome this rejection. None of these amendments changes the scope of the claims. They merely clarify the original scope of the claims.

In claims 20, 21, 33, 35, 40 and 47, and the claims that depend therefrom, applicants have replaced "homologous" with "sequence identity".

In claim 20 (which the Examiner referred to as claim 1), applicants have replaced "having" with "comprising". Applicants have made a similar amendment in claims 21, 33, 35, 40 and 47 and the claims that depend therefrom.

In claims 20, 21, 33, 35, 40 and 47, applicants have amended the claim language to indicate clearly that plasmid "pNB2" was deposited as DSM 9196.

Based on the foregoing amendments, applicants request that the Examiner withdraw the rejections of claims 20-21, 33-38, 40-41 and 47 under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 112, First Paragraph

Written Description

The Examiner has rejected claims 20-21, 33–38 , 40–41, and 47 under 35 U.S.C. § 112, first paragraph. He argues that the specification lacks a written description of the invention. The Examiner acknowledges that applicants isolated a nucleic acid encoding an amylosucrase and expressed it to produce amylosucrase. However, the Examiner argues that the application does not identify structural features unique to the *Neisseria polysaccharea* amylosucrase, functional domains of the protein, or its overall function. The Examiner also argues that it remains unclear what features identify an *Neisseria polysaccharea* amylosucrase protein or a DNA sequence that has 60% sequence identity with the specific DNA sequences listed in the claims. Applicants traverse.

The specification, as filed, provides a complete written description of the subject matter of the pending claims.

The "first" DNA sequence of the claims characterizes the claimed methods. It is defined as a sequence having more than 60% sequence identity to various specific sequences. These specific sequence are:

a. the sequence coding for a protein comprising SEQ ID NO.2 -- a specific sequence;
b. the coding region SEQ ID NO.1 -- a specific sequence;
c. the "amylosucrase" DNA sequence of plasmid pNB2 (DSM 9196) -- a specific sequence;
d. the DNA sequence coding for a protein encoded by the DNA insert of plasmid pNB2 (DSM 9196) -- a specific sequence;
e. a part of any of the specific sequences (a), (b), (c) or (d) -- a specific sequence;
f. the compliment of (a), (b), (c), (d) or (e) -- a specific sequence.

Each of those specific sequences are described in the specification -- SEQ ID NO.1 (page 4, lines 28-32; pages 39-42); SEQ ID NO.2 (pages 42-44); and pNB2 (DSM 9196) (page 30, lines 5-7 and Figure 1).

Thus, without the "60% sequence identity", there could be no issue of lack of written description. That term, however, does not cause the claim to lack written description. First and foremost, the scope of the term is specifically recited in the specification. Thus, there is no question that applicants had possession of an invention of the claimed scope when they filed the application. Second, the Federal Circuit in cases post - *Regents v. Lilly* have both recognized the written description inherent in deposits and in sequence relatedness language.

> "[R]eference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of §112, 1" *Enzo Biochem, Inc. v. Gen-Probe Incorporated,* 323 F.3d 956, 964 (Fed. Cir. 2002).
>
> "[A]n adequate written description of genetic material 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' ". *Id.* at 964.

> "[T]he special case of the biological deposit is a method of complying with the statutory requirements" *Id.* at 975.

The PTO Written Description Guidelines (cited with approval in Enzo) state that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed relevant identifying characteristics ... *i.e.*, complete or partial structure." *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement,* 66 Fed. Reg. 1099, (Jan. 5, 2001), 1106 ("*Guidelines*").

The *Guidelines* also make plain that claims reciting "hybridization" or sequence relatedness does not lack written description. *See*, e.g., Example 9. In Example 9, a claim to a DNA that hybridizes (i.e., has a sequence homology) to a DNA whose sequence was determined and recited (SEQ ID NO:1) was stated to satisfy the written description requirement. As the *Guidelines* state: "a person of skill in the art would not expect substantial variations among the [claimed] species ... Thus, a representative number of species is disclosed ... and the level of skill or knowledge in the art are adequate to determine the applicant was in possession of the claimed invention."

Accordingly, applicants request that the Examiner reconsider and withdraw the written description rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

Enablement

Claims 20-21, 33-38, 40-41 and 47 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner acknowledges that applicants disclose the isolation of a *N. polysaccharea* genomic sequence and the expression of an amylosucrase using that sequence in *E. coli*. The Examiner acknowledges that the amylosucrase was

detected in *E. coli* and that soluble and insoluble products were detected in the growth medium and that the soluble products were short-chained polysaccharides. The Examiner, however, argues that applicants have not enabled a method of producing linear α-1,4 glucans, fructose and/or fructose syrup in (a) a culture medium comprising bacteria comprising a DNA sequence that exhibits more than 60% sequence identity to the various sequences of the pending claims, or (b) a plant transformed with those sequences of the encoded protein that is targeted to a vacuole or to the apoplast. Applicants traverse.

There are two prongs to the Examiner's rejection. Both are flawed and not supported by the art and are contrary to the enabling disclosure of the specification.

First, the Examiner's enablement rejection posits that only the specific DNA of SEQ ID NO.1, the insert of plasmid pNB2, or full length complements of those sequences will produce a functional amylosucrase. That is just not correct. There is absolutely no basis to believe that the overwhelming majority of DNA sequences that have more than 60% sequence identity to the specific DNA sequences of the claims will not produce a functional amylosucrase. In fact, the skilled worker would not only expect the vast majority of those DNAs to produce functional amylosucrase but be surprised if they did not have that activity. Further, the pending claims require the protein produced have that specific activity. And, the specification and the art provide specific assays for confirming the activity.

Neither Bowie et al., *Science*, 247 pp. 1306-10 (1990) (hereinafter "Bowie"), nor McConnell et al., *Nature*, 411, pp. 709-713 (2001) (hereinafter "McConnell") change the expectation of the skilled worker that the vast majority of amino acid substitutions do not significantly affect the activity of a protein.

Bowie, for example, reports that the amino acid sequence encoded message for protein shape and function is "highly degenerate in that many different sequences can code for proteins with essentially the same structure and activity" (Abstract). Likewise, it reported that in the context of the lac repressor more than one-half of the substitutions at 142 different positions had no effect on function and many of the others were also acceptable, *i.e.*, conservation substitutions (p. 1306). Finally, Bowie reports that it is "possible to use genetic methods to generate lists of allowed amino acid substitutions" (p. 1310).

McConnell is consistent with Bowie's observations. It shows that single amino acid changes can have an effect on activity. It does not show that the vast majority of such changes would also have any effect on activity. The reason is simple -- they would not and do not.

Were the Examiner's concerns shared by the skilled worker, and others in the PTO, claims reciting hybridization, homology or sequence identity would all be invalid for lack of enablement. Of course, that is not the case. These claims routinely issue from the PTO and from patent office all over of the world. And, they are routinely accepted by the art and upheld by the Courts. *See, Enzo Biochem, Inc. v. Gen-Probe Incorporated,* 323 F.3d 956, 964 (Fed. Cir. 2002).

Second, the Examiner's enablement rejection posits that even a functional amylosucrase does not "always produce the expected results." Again, the Examiner's position is at odds with the facts.

All of the documents on which the Examiner purports to rely show that amylosucrase does synthesize linear α-1,4 glucans and that the formation of α-1,4 glucans is the main reaction product of amylosucrase from sucrose. For example, Remaud-Simeon et

al., "Studies on a Recombinant Amylosucrase," Carbohydrate bioengineering. Proc. Int. Conf. Elsinore, Denmark, *Prog. Biotechnol.* 10:313-320, 1995 (hereinafter "Remaud-Simeon"), emphasizes that the polymer produced in a reaction of a purified amylosucrase in the presence of sucrose and glycogen was "confirmed ...[to be] a glucopolysaccharide composed of alpha-1,4 linkages. No traces of alpha-1,6 branched linkages could be detected" (p.317). Remaud-Simeon also states, that "[f]ructose is the only reducing sugar detected in the presence of glycogen and starch" (p.318).

The Examiner acknowledges, as he must, that the cited documents "support Applicants' demonstration that a nucleic acid molecule isolated from Neisseria bacteria encodes a amylosucrase that can be used to produce α-1,4 glycans." Given the well-recognized conservation in protein function of the vast majority of amino acid substitutions (*see* discussions above), there is no reason to believe that the vast majority of amylosucrases encoded for by the DNA sequences claimed (*i.e.*, those having more than 60% sequence identity to the recited sequences) would not perform in the same way to produce α-1,4 glycans

With respect to the production of α-1,4 glycans by amylosucrase in plants, it is well known that sucrose is a central metabolite of plants. See, Quick and Schaffer in Zamski and Schaffer, 1996, "Photoassimilate Distribution In Plants And Crops: Source–Sink Relationships", Chapter 6, Marcel Dekker Inc., New York, (hereafter "Quick and Schaffer"). As detailed in the March 24, 2003 Amendment and Response to Office Action, Quick and Schaffer teach that "[s]tarch and sucrose are the major end-products of photosynthesis." (line 1 of the Introduction). Further, "[t]he phenomenon of sugar accumulation in sinks [(*e.g.* storage organs)], is widespread, and some of the most important agronomic crops are those that accumulate large amounts of sugar, particularly sucrose." (page 125, lines 42–45).

Thus, contrary to the Examiner's allegations, plants do store sucrose and thus the storage sucrose would be utilized in the claimed invention.

In view of this state of the art, the well recognized practice of the USPTO, and the teachings of the specification there can be no doubt that one of ordinary skill in the art could make and use the claimed invention without undue experimentation and with a reasonable expectation of success. Applicants, therefore, request that the Examiner reconsider and withdraw the rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

Deposit

The Examiner has rejected claims 20-21, 33–38 , 40–41, and 47 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner argues that the specification does not disclose a repeatable process to obtain the exact same plasmid in each occurrence and it is not apparent if such a plasmid is readily available to the public. Applicants traverse.

In accordance with 37 C.F.R. § 1.808, the plasmid pNB2 of the invention was deposited at Deutsche Sammlung von Mikroorganismen (DSM), Braunschweig, Germany, on May 6, 1994 according to the provisions of the Budapest Treaty under Deposit No. 9196. All restrictions were removed upon granting of a patent in the parent application to this divisional application -- US Patent No. 6,265,635 B1 (July 24, 2001). *See* the May 10, 1999 "Statement

Verifying Unrestricted Access to Deposited Biological Material Upon Grant of Patent" (Exhibit A). Thus, the deposit requirement has been satisfied.

CONCLUSION

Applicants request that the Examiner consider the foregoing remarks and allow the pending claims to issue. If the Examiner believes that a telephonic interview would be helpful, he is invited to call the undersigned at any time.

Respectfully submitted,

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GFB-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner	:	Ousama M-Faiz Zaghmout
Group Art Unit	:	1649
Applicants	:	Jens Kossmann et al.
Serial No.	:	08/737,752
Filed	:	February 27, 1997
For	:	DNA SEQUENCES CODING FOR ENZYMES CAPABLE OF FACILITATING THE SYNTHESIS OF LINEAR α-1,4 GLUCANS IN PLANTS, FUNGI AND MICROORGANISMS

New York, New York
May 10, 1999

Honorable Assistant Commissioner
for Patents
Washington, D.C. 20231

STATEMENT VERIFYING UNRESTRICTED ACCESS TO DEPOSITED BIOLOGICAL MATERIAL UPON GRANT OF PATENT

Sir:

In accordance with 37 C.F.R. § 1.808, I hereby state that all restrictions on the public availability of the deposited material, plasmid pNB2 deposited at Deutsche Sammlung von Mikroorganismen (DSM), Braunschweig, Germany on May 6, 1994 under

Deposit No. DSM 9196, will be irrevocably removed upon the granting of a patent in the above-identified application.

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I Hereby Certify that this Correspondence is being Deposited with the U.S. Postal Service as First Class Mail in an Envelope Addressed to: ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231 on

May 16, 1997

Claire J. Saintil

Signature of Person Signing